

REMARKS

Claims 1, 4-7, 9-10, 12-14, 42, and 45 are pending. The Applicant herein respectfully requests further examination of the application and reconsideration of the claims, in view of the amendments and remarks presented herein. The Applicants have amended the Title of the Invention as recommended by the Examiner.

ISSUES UNDER 35 USC §112, PARAGRAPH 2

The Applicant herewith presents amendments to claim 1 to clarify the language highlighted by the Examiner.

Claim 1 is indeed drawn toward a method for directly monitoring volatile compounds in a gas or vapor phase medium from a nucleic acid enzymatic reaction, during the reaction. However, the claimed method is not drawn toward the reaction, *per se*. Accordingly, steps of an enzymatic reaction, *per se*, as requested by the Examiner, are not relevant to the subject matter of the claimed invention. Indeed the claimed method is a method of monitoring volatile compounds associated with nucleic acids and products thereof during a reaction, not the reaction.

Claim 1 is now further amended to address the Examiner's issues raised with regard to the antecedent basis of the subject matter of claims 13 and 14.

Claim 45 is amended to now recite the term "subsequently" to particularly point out the order of the process.

The Applicant respectfully requests the Examiner to withdraw the rejections.

REJECTIONS UNDER 35 USC §102

Claims to the present invention stand rejected as allegedly anticipated under 35 USC §102(e) by the disclosure of either the Van Ness ('893) patent or the published application, Koster ('394).

A. Van Ness '893 "Methods and compositions for determining the sequence of nucleic acid molecules"

The Applicant respectfully highlights to the Examiner that an express necessity of all embodiments of sequencing methods contemplated within the scope of Van Ness require, before detection, "separation of the tagged [nucleic acid] fragments by sequential length", i.e., the same necessary step of conventional sequencing. See, e.g., '893 Abstract; Summary of the Invention (col.5, line 6); Detailed Description (col.17, lines 52-54; col.45, line 54, *et seq.*). The Van Ness '893 disclosure provides a method for sequencing nucleic acids that fundamentally and necessarily requires, in the order, 1) separation of nucleic acid fragments according to size, 2) cleavage of a tag from the nucleic acid, and 3) detection of the tag. The Examiner is respectfully referred to the unambiguous language of the '893 disclosure, beginning at col.45, entitled "Sequencing Methods and Strategies", wherein the description requires, "[f]ollowing generation of tagged nucleic acid fragments, the tagged fragments are separated by sequential length. Such separation may be performed by a variety of techniques." Col. 46, line 11, *et seq.* The Van Ness '893 disclosure, beginning at col.52, line 33, describes the necessarily required step of "Separation of DNA Fragments", e.g., by conventional electrophoresis.

In sharp contrast, the Applicant respectfully points out to the Examiner that the method of the present invention is directed to a real time method for *directly* monitoring a gas or vapor phase medium from a nucleic acid enzymatic reaction, *during* the reaction.

Accordingly, since none of the claims presented herewith encompass any embodiment within the disclosure of Van Ness, the '893 disclosure cannot, as a matter of law, anticipate the subject matter of any of the claims.

The Applicant therefore respectfully request the Examiner to withdraw the rejection under 35 USC §102 in view of Van Ness '893.

B. Koster ('394) "Automated Process Line"

The Examiner is respectfully reminded that an anticipatory reference must teach an embodiment, *per se*, that falls within the scope of the Applicant's claims to Anticipate under 35 USC §102. Particularly, under the Patent Statutes, i.e., §§ 102/112.1, Anticipation fundamentally requires that an anticipatory reference must unequivocally demonstrate possession of the claimed subject matter in the art before the Applicant's invention. Similarly, the alleged anticipatory reference must fundamentally teach how to make and use an embodiment within the scope of the

claims. However, although Koster contemplates a robotic analytical system to integrate a myriad of possible instrumentalities, i.e., “[a] fully automated modular analytical system integrates instrumentation to permit analysis of biopolymer samples”, and this all-encompassing language is used throughout the published application, no embodiments are described or enabled under 35 USC §112.1 that fall within the scope of any of the Applicant’s claims. Particularly, Koster does not teach or contemplate a method for *directly* monitoring volatile compounds in a gas or vapor phase medium from a nucleic acid enzymatic reaction *during* that reaction.

Koster paragraph 81, cited by the Examiner, for example, merely contemplates sequencing and diagnostics based on analysis of nucleic acids and polypeptides or diagnostics by mass spectrometry. Koster paragraphs 108-125, as cited by the Examiner, merely contemplate a system in abstract terms that can evaluate a solid-phase reaction by means of mass spectrometry, *after* the reaction is completed. Koster, however, does not describe any embodiments that fall within the Applicant’s claims. In order for an asserted reference to anticipate a claimed invention that reference must unequivocally indicate possession of at least one embodiment within the scope of the claims at issue. Moreover, for an asserted reference to anticipate a claimed invention, that reference must also teach how to make and use at least one embodiment within the scope of the claims at issue. Koster does not, however, contemplate directly monitoring volatile compounds using a real time single-stop multisensor array in a gas or vapor phase medium of a nucleic acid reaction. The Koster robotic systems are designed such that they can be integrated with other computer-controlled instrumentation to perform a series of operations to effect a multi-step process, i.e., “automated process line”.

Since none of the Applicant’s claims encompass any embodiment within the disclosure of Koster, the Applicant respectfully submits that Koster (‘394), as a matter of law, cannot anticipate any of the claims to the present invention. The Applicant, accordingly, respectfully requests the Examiner to withdraw the rejection.

Rejections under 35 USC §103

Claims 4-6 and 45 are rejected as obvious in view of Van Ness ('893) combined with Freidhoff ('115) or Van Ness ('893) combined with Koster ('394).

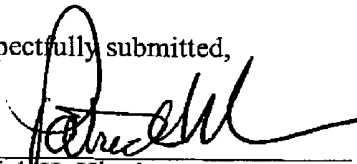
The Examiner is respectfully reminded that to establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all the claim limitations. Van Ness et al is alleged to teach the claimed method and Freidhoff et al is alleged to teach a multisensor array comprising a metal oxide gas sensor that would be obvious to employ in combination with the teachings of Van Ness. The Examiner is first respectfully referred to the distinction from Van Ness highlighted *supra*. Particularly, the '893 disclosure provides a method for sequencing nucleic acids that fundamentally and necessarily requires, in the order, 1) separation of nucleic acid fragments according to size, 2) cleavage of a tag from the nucleic acid, and 3) detection of the tag. The method of the present invention does not require separation of nucleic acid fragments according to size. Accordingly, even if Freidhoff supplied all of the other elements of the claims and if someone of ordinary skill were motivated to combine the references, the subject matter of the Applicant's claims still would not be reached. Freidhoff ('115) issued January 1995. Van Ness ('893), however, was not even filed until July 1997. Indeed, Van Ness had thirty (30) months to study the Freidhoff ('115) disclosure to incorporate any aspect that may be useful to employ. Moreover, the universe of skilled individuals, including Koster, had the opportunity to conceive and/or reduce to practice the invention now claimed by the applicant in view of these disclosures. However, no one did. The specific combination now claimed by the Applicant was not even contemplated by those of skill in the art working to solve the same problem. It is axiomatic that a claimed invention is not obvious solely because it is composed of elements that are all individually found in the prior art. *See, e.g., In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998).

The Applicant respectfully requests the Examiner to withdraw the rejections.

For all the foregoing reasons, the Applicant submits that Claims 1, 4-7, 9-10, 12-14, 42, and 45 are in condition for allowance. Early action toward this end is courteously solicited. The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.

The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,



Patrick H. Higgins
Reg. No. 39,709
Attorney for Applicant

DATE: May 20, 2004

MATHEWS, COLLINS, SHEPHERD & McKAY, P.A.
100 Thanet Circle, Suite 306
Princeton, New Jersey 08540-3662
Telephone: (609) 924-8555
Facsimile: (609) 924-3036